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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/715,172	11/20/2000	Hideaki Suzuki	2167-0116P	6879

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EXAMINER	
DO, PENSEE T	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 03/12/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/715,172	Applicant(s) SUZUKI ET AL.	
	Examiner Pensee T. Do	Art Unit 1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 December 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) *11-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6-7* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Amendment Entry

1. The amendment filed on December 20, 2001 has been acknowledged and entered as paper no. 8.

Withdrawn Rejection(s)

2. Rejection under 35 USC 112, 2nd paragraph is withdrawn herein.

Objection to the specification is also withdrawn herein.

Maintained Rejection(s)

Claim Rejections - 35 U.S.C. § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 1, 8-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Aoki et al. (Clinica Chimica ACTA(Dec 15 1988) 178(2) 193-204) in view of Voet et al. (Biochemistry 1990).

Aoki teaches an enzyme immunoassay of medullasin in peripheral blood. Medullasin is located in granulocytes (leukocytes) and bone marrow cells. The medullasin protein is extracted and purified for antibody generation in rabbits. A solid support is coated with an anti-medullasin IgG antibody. The coated bead is incubated with an amount of diluted

peripheral blood to bind the medullasin. After incubation, the complex is incubated with an enzyme labeled conjugate and the amount of activity of the label is determined (pages 195-196).

However, Aoki does not teach using an aqueous liquid for lysing cells. Voet teaches isolation of protein located in cytosol of cells by osmolysis. Isolation of protein requires that the protein is in solution. Therefore, cells are suspended in a hypotonic solution and under the influence of osmotic forces, water diffuses into the more concentrated intracellular solution thereby causing the cells to swell and burst thus releasing the protein of interest (page 76).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Aoki by suspending cells comprising the protein of interest into a buffer solution having an osmotic pressure sufficient to allow osmolysis of the cell as taught in the method of Voet because Voet teaches that osmolysis of cells for protein isolation is conventional in the art and is efficient, simplest, and gentlest method known.

5. Claims 2-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Aoki in view of Voet as applied to claims 1, 8-10 above and further in view of Lapicola (US 4,745,071).

See discussion on Aoki and Voet set forth above. These references differ from the invention in failing to teach a specific buffer or lysing agent for cells. Lapicola teaches a method for the volumeric differentiation of blood cell types. The reagents used comprise a diluent with an osmolality that can be adjusted to 320 +/-5 milliosmoles with sodium

chloride. The level of the diluent can be set at a level other than 320 +/- 5 milliosmoles. The organic buffers comprise various acids and alcohols (col. 5, lines 35-55). A surfactant such as quaternary ammonium salts comprising three alkyl short chain groups may be added to the diluent as a lysing agent. The studies of the quaternary ammonium salts in blood show lysing of various leukocyte populations (col. 6, lines 32-68).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate in the modified method of Aoki the buffers comprising lysing reagent as taught in the method of Lapicola because Lapicola teaches that quaternary salts disclosed in the diluent buffers were capable of lysing leukocyte populations in blood. Therefore, one would have been motivated to incorporate a solution comprising a surfactant such as a quaternary salt for lysing of leukocytes for the quantification of medullasin activity in a blood sample.

Response to Arguments

Applicant's arguments filed on December 20, 2001 have been fully considered but they are not persuasive.

Applicants argue that one of ordinary skill in the art would not be motivated by either reference to lyse leukocytes prior to determining the amount of medullasin in the patient sample because Voet fails to teach the treatment of the present invention for the analysis of medullasin content.

Since Aoki teaches that the polystyrene balls coated with IgG were incubated with various amounts of medullasin or peripheral blood diluted with 0.1 mol/1 sodium phosphate buffer, the lysing step is inherently taught through the dilution of the

peripheral blood. Thus, one of ordinary skill in the art would be motivated to lyse the cells in the blood sample according to such method taught by Voet. Voet's method can be applied to any type of cells regardless of what in the cell is being detected. After all, medullasin is a protein present in the cells.

Applicants also argue that Voet does not teach the limitation of using an aqueous liquid having the osmotic pressure, 250 mOsm/kg.H_2O or less, or to 310 mOsm/kg H_2O or more.

Voet teaches osmotic lysis using detergents or organic solvents such as acetone or toluence are useful in lysing cells (see page 76, col.2 par. 2, lines 1-16). One of ordinary skills in the art would be able to arrive at a suitable osmotic pressure through routine experimentation to efficiently break up the leukocytes.

Applicants also argue that Aoki teaches a non-lysing method which claimed to give the result that is well correlated with the values correlated from the protease activity measured by conventional methods.

As mentioned above, Aoki teaches that the peripheral blood is diluted in a buffer, NaCl (salt) or BSA, which are organic solvents and Voet teaches that organic solvents are used as lytic solutions. Thus, Aoki does not teach away from lysing the cells in the blood sample.

Applicants mentioned that the references fail to teach the limitation of claim 10 which requires that the anti-human medullasin is a monoclonal antibody.

It would have been obvious to one of ordinary skills in the art to use a monoclonal antibody for its specificity.

Regarding the rejections of claims 2-7 by Aoki in view of Voet and Lapicola, applicants point out the distinctions between the present invention and the references Aoki and Voet and argues that the Lapicola reference does not cure the deficiencies in the examiner's rejection.

Since Aoki and Voet have been discussed above to cure the deficiencies, no further discussion is need on the Lapicola reference. The rejection for claims 2-7 is still maintained.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pensee T. Do whose telephone number is (703) 308-4398. The examiner can normally be reached on Mon-Fri. from 7 a.m. to 3 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (703) 305-3399. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Pensee T. Do

Patent Examiner

3/10/02

LONG V. LE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600
03/11/02